

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: RITA MITRA Examiner #: 77995 Date: 3/21/02
Art Unit: 1653 Phone Number 301 605-1211 Serial Number: 09/466778
Mail Box and Bldg/Room Location: 980/CMT/ Results Format Preferred (circle) PAPER DISK E-MAIL
En 9803

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: "Novel Hyaluronan-binding proteins and encoding genes"
Inventors (please provide full names): Gregg Hastings, Gene Liao, Elena Tsiferina
Earliest Priority Filing Date: 12/23/1998

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

1. I would request an Author Search : See attached Ref. Q9NR Y3 (Seq. Search Result of Tao Q., Zhang W., Cao X).

2. A search on human FELL Protein or CD44-like Precursor FELL

Keywords : Hyaluronan-binding domain/motif
Hyaluronic acid binding protein
FELL
CD44

Point of Contact:
Barb O'Brien
Technical Information Specialist
STIC CM1 6A05 308-4291

STAFF USE ONLY

| | Type of Search | Vendors and cost where applicable |
|--|------------------------|-----------------------------------|
| Searcher: <u>for B</u> | NA Sequence (#) _____ | STN <u>319</u> |
| Searcher Phone #: _____ | AA Sequence (#) _____ | Dialog _____ |
| Searcher Location: _____ | Structure (#) _____ | Questel/Orbit _____ |
| Date Searcher Picked Up: _____ | Bibliographic <u>X</u> | Dr.Link _____ |
| Date Completed: <u>3-25-02</u> | Litigation _____ | Lexis/Nexis _____ |
| Searcher Prep & Review Time: <u>25</u> | Fulltext _____ | Sequence Systems _____ |
| Clerical Prep Time: _____ | Patent Family _____ | WWW/Internet _____ |
| Online Time: <u>47</u> | Other _____ | Other (specify) _____ |

THIS PAGE BLANK (USPTO)

=> stnindex

ENTER FILE OR CLUSTER NAMES (NONE):allbib

INDEX '1MOBILITY, 2MOBILITY, ADISALERTS, AEROSPACE, AGRICOLA, ALUMINIUM,
ANABSTR, AQUASCI, BABS, BIBLIODATA, BIOBUSINESS, BIOCOMMERCE, BIOSIS,
BIOTECHABS, BIOTECHDS, BIOTECHNO, BLLDB, CABA, CANCERLIT, CAPLUS, CBNB,
CEABA-VTB, CEN, CERAB, CHEMSAFE, CIN, ...' ENTERED AT 09:52:55 ON 25 MAR 2002

123 FILES IN THE FILE LIST IN STNINDEX

Enter SET DETAIL ON to see search term postings or to view
search error messages that display as 0* with SET DETAIL OFF.

=> s fell(2a)(protein# or peptide# or polypeptide# or precursor#)

1 FILE 1MOBILITY
2 FILE ADISALERTS
2 FILE AEROSPACE
16 FILE AGRICOLA
15 FILE AQUASCI
7 FILE BABS
14 FILE BIOBUSINESS
331 FILE BIOSIS
8 FILE BIOTECHABS
8 FILE BIOTECHDS
68 FILE BIOTECHNO

16 FILES SEARCHED...

384 FILE CABA
67 FILE CANCERLIT
476 FILE CAPLUS
3 FILE CBNB
1 FILE CIN
1 FILE COMPENDEX

27 FILES SEARCHED...

1 FILE COMPUAB
5 FILE CROPU
50 FILE DDFU

41 FILES SEARCHED...

276 FILE DRUGU
283 FILE EMBASE
1 FILE ENCOMPLIT
1 FILE ENCOMPLIT2
63 FILE ESBIODBASE

55 FILES SEARCHED...

4 FILE EUROPATFULL
7 FILE FROSTI
45 FILE FSTA
1 FILE GENBANK

62 FILES SEARCHED...

5 FILE INVESTEXT
10 FILE IPA
6 FILE JICST-EPLUS

76 FILES SEARCHED...

46 FILE LIFESCI
302 FILE MEDLINE
4 FILE NIOSHTIC
11 FILE NLDB

85 FILES SEARCHED...

4 FILE NTIS
1 FILE OCEAN
49 FILE PASCAL

90 FILES SEARCHED...

93 FILES SEARCHED...

30 FILE PCTFULL

7 FILE PHIN
1 FILE POLLUAB
25 FILE PROMT
164 FILE SCISEARCH
104 FILES SEARCHED...
109 FILES SEARCHED...
116 FILE TOXCENTER
35 FILE USPATFULL
117 FILES SEARCHED...
3 FILE WPIDS
3 FILE WPINDEX

48 FILES HAVE ONE OR MORE ANSWERS, 123 FILES SEARCHED IN STNINDEX

L1 QUE FELL(2A)(PROTEIN# OR PEPTIDE# OR POLYPEPTIDE# OR PRECURSOR#)

=> s (tao q?/au or zhang w?/au or cao x?/au or tao, q?/au or zhang, w?/au or cao, x?/au)
and l1

0* FILE BIOCOMMERCE
15 FILES SEARCHED...
19 FILES SEARCHED...
0* FILE CBNB
0* FILE CIN
29 FILES SEARCHED...
41 FILES SEARCHED...
0* FILE DRUGNL
55 FILES SEARCHED...
60 FILES SEARCHED...
1 FILE GENBANK
0* FILE IFICLS
71 FILES SEARCHED...
77 FILES SEARCHED...
0* FILE NLDB
87 FILES SEARCHED...
0* FILE PATDPA
95 FILES SEARCHED...
0* FILE PHIC
0* FILE PHIN
107 FILES SEARCHED...
120 FILES SEARCHED...

- this is the record retrieved in the seq. search

1 FILES HAVE ONE OR MORE ANSWERS, 123 FILES SEARCHED IN STNINDEX

L2 QUE (TAO Q?/AU OR ZHANG W?/AU OR CAO X?/AU OR TAO, Q?/AU OR ZHANG, W?/AU O
R CAO, X?/AU) AND L1

=> FILE CANCERLIT, MEDLINE, PASCAL, JICST-EPLUS, CABA, DRUGU, CAPLUS, BIOSIS, BIOTECHNO, ESBIODBASE, CONFSCI, LIFESCI, EMBASE
FILE 'CANCERLIT' ENTERED AT 10:28:45 ON 25 MAR 2002

FILE 'MEDLINE' ENTERED AT 10:28:45 ON 25 MAR 2002

FILE 'PASCAL' ENTERED AT 10:28:45 ON 25 MAR 2002
Any reproduction or dissemination in part or in full,
by means of any process and on any support whatsoever
is prohibited without the prior written agreement of INIST-CNRS.
COPYRIGHT (C) 2002 INIST-CNRS. All rights reserved.

FILE 'JICST-EPLUS' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 Japan Science and Technology Corporation (JST)

FILE 'CABA' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 CAB INTERNATIONAL (CABI)

FILE 'DRUGU' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

FILE 'CAPLUS' ENTERED AT 10:28:45 ON 25 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'BIOTECHNO' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'ESBIODBASE' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V., Amsterdam. All rights reserved.

FILE 'CONFSCI' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 Cambridge Scientific Abstracts (CSA)

FILE 'LIFESCI' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 Cambridge Scientific Abstracts (CSA)

FILE 'EMBASE' ENTERED AT 10:28:45 ON 25 MAR 2002
COPYRIGHT (C) 2002 Elsevier Science B.V. All rights reserved.

=> d que 110; d que 113; d que 117
L3 961 SEA TAO Q?/AU
L4 22455 SEA ZHANG W?/AU
L5 4699 SEA CAO X?/AU
L6 83 SEA L3 AND L4 AND L5
L7 23481 SEA CD44 OR CD 44
L8 232730 SEA FELL
L9 80395 SEA HYALURON?
L10 0 SEA L6 AND (L7 OR L8 OR L9)

L7 23481 SEA CD44 OR CD 44
L8 232730 SEA FELL
L13 0 SEA L7(5A) L8

L7 23481 SEA CD44 OR CD 44
L8 232730 SEA FELL
L16 281 SEA L7 (10A) PRECURSOR#
L17 0 SEA L16 (10A) L8

=> d que 16

L3 961 SEA TAO Q?/AU
L4 22455 SEA ZHANG W?/AU
L5 4699 SEA CAO X?/AU
L6 83 SEA L3 AND L4 AND L5

- references containing all 3 inventors & author names, regardless of topic

=> dup rem 16

PROCESSING COMPLETED FOR L6

L27 36 DUP REM L6 (47 DUPLICATES REMOVED)
ANSWERS '1-8' FROM FILE CANCERLIT
ANSWERS '9-11' FROM FILE MEDLINE
ANSWERS '12-34' FROM FILE CAPLUS
ANSWERS '35-36' FROM FILE BIOSIS

=> d ibib ab 127 1-36

L27 ANSWER 1 OF 36 CANCERLIT
ACCESSION NUMBER: 2000161143 CANCERLIT
DOCUMENT NUMBER: 20161143
TITLE: Adenovirus-mediated lymphotactin gene transfer improves therapeutic efficacy of cytosine deaminase suicide gene therapy in established murine colon carcinoma.
AUTHOR: Ju D W; **Tao Q**; Cheng D S; **Zhang W**; Zhang M; Hamada H; **Cao X**
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, PR China.
SOURCE: GENE THERAPY, (2000). Vol. 7, No. 4, pp. 329-38. Journal code: CCE. ISSN: 0969-7128.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 20161143
ENTRY MONTH: 200004

DUPLICATE 1

L27 ANSWER 2 OF 36 CANCERLIT
ACCESSION NUMBER: 1999393970 CANCERLIT
DOCUMENT NUMBER: 99393970
TITLE: Enhanced antitumor immune responses of IL-2 gene-modified tumor vaccine by combination with IL-1 and low dose cyclophosphamide.
AUTHOR: **Cao X**; **Zhang W**; Wan T; Yu Y; **Tao Q**; Wang J
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, P.R. China.
SOURCE: JOURNAL OF EXPERIMENTAL AND CLINICAL CANCER RESEARCH, (1999). Vol. 18, No. 2, pp. 173-9. Journal code: CUI. ISSN: 0392-9078.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99393970
ENTRY MONTH: 199911
AB To enhance the antitumor immunity induced by IL-2 gene-modified tumor vaccine, we proposed a combined protocol to treat tumor-bearing mice using IL-2 gene-modified tumor vaccine in combination with IL-1 and low-dose

DUPLICATE 3

Cyclophosphamide (Cy). After treatment with IL-2 gene-modified B16 melanoma cell vaccine alone, the pulmonary metastases of tumor-bearing mice were reduced and their survival time was prolonged. The anti-metastases effect was improved when the vaccine was used in combination with IL-1 or low-dose Cy. The best therapeutic effect was achieved when the IL-2 gene-modified vaccine was combined with IL-1 and low-dose Cy. The cytotoxicity of the splenic CTL, NK, and the levels of IL-2, TNF secreted by splenocytes increased after tumor-bearing mice were treated with the IL-2 gene-modified tumor vaccine. The above antitumor immune functions were augmented more significantly when IL-1, low-dose Cy were used in combination with IL-2 genemodified tumor vaccine. These results demonstrated that the IL-2 gene modified vaccine could exert more potent anti-metastases effects when it is combined with IL-1 or/and low-dose Cy by activating the specific and non-specific antitumor immune responses more effectively.

L27 ANSWER 3 OF 36 CANCERLIT
ACCESSION NUMBER: 1999049857 CANCERLIT
DOCUMENT NUMBER: 99049857
TITLE: Lymphotactin gene-modified bone marrow dendritic cells act as more potent adjuvants for peptide delivery to induce specific antitumor immunity.
AUTHOR: Cao X; Zhang W; He L; Xie Z; Ma S; Tao Q; Yu Y; Hamada H; Wang J
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, People's Republic of China.
caoxt@public3.sta.net.cn
SOURCE: JOURNAL OF IMMUNOLOGY, (1998). Vol. 161, No. 11, pp. 6238-44.
Journal code: IFB. ISSN: 0022-1767.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Abridged Index Medicus Journals; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99049857
ENTRY MONTH: 199901

AB Dendritic cells (DC) are regarded as attractive candidates for cancer immunotherapy. Our aim is to improve the therapeutic efficacy of DC-based tumor vaccine by augmenting DC preferential chemotaxis on T cells. Mouse bone marrow-derived DC were transduced with lymphotactin (Lptn) gene by adenovirus vector. The supernatants from Lptn gene-modified DC (Lptn-DC) were capable of attracting CD4+ and CD8+ T cells in a chemotaxis assay, whereas their mock control could not. Lptn expression of Lptn-DC was further confirmed by RT-PCR. Lptn-DC were pulsed with Mut1 peptide and used for vaccination. Immunization with the low dose (1×10^4) of Mut1 peptide-pulsed DC induced weak CTL activity, whereas the same amounts of Mut1 peptide-pulsed Lptn-DC markedly induced specific CTL against 3LL tumor cells. A single immunization with 1×10^4 Mut1 peptide-pulsed Lptn-DC could render mice resistant to a 5×10^5 3LL tumor cell challenge completely, but their counterpart could not. The protective immunity induced by Mut1 peptide-pulsed Lptn-DC depends on both CD4+ T cells and CD8+ T cells rather than NK cells in the induction phase and depends on CD8+ T cells rather than CD4+ T cells and NK cells in the effector phase. Moreover, the involvement of CD28/CTLA4 costimulation pathway and IFN-gamma are also necessary. When 3LL tumor-bearing mice were treated with 1×10^4 Mut1 peptide-pulsed Lptn-DC, their pulmonary metastases were significantly reduced, whereas the same low dose of Mut1 peptide-pulsed DC had no obvious therapeutic effects. Our data suggest that Lptn-DC are more potent adjuvants for peptide delivery to induce protective and therapeutic antitumor immunity.

L27 ANSWER 4 OF 36 CANCERLIT
ACCESSION NUMBER: 1999257887 CANCERLIT

DOCUMENT NUMBER: 99257887
TITLE: Adenovirus-mediated GM-CSF gene and cytosine deaminase gene transfer followed by 5-fluorocytosine administration elicit more potent antitumor response in tumor-bearing mice.
AUTHOR: Cao X; Ju D W; Tao Q; Wang J; Wan T; Wang B M; Zhang W; Hamada H
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, PR China.
SOURCE: GENE THERAPY, (1998). Vol. 5, No. 8, pp. 1130-6.
Journal code: CCE. ISSN: 0969-7128.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 99257887
ENTRY MONTH: 199907

AB Antitumor effects of combined transfer of suicide and cytokine genes were investigated in this study. Adenovirus harboring E. coli cytosine deaminase gene (AdCD) and adenovirus harboring murine granulocyte-macrophage colony-stimulating factor gene (AdGMCSF) were used simultaneously for in vivo gene transfer in melanoma-bearing mice. Growth inhibition of established tumors and prolongation of survival period were observed more significantly in tumor-bearing mice after transfection with AdGMCSF and AdCD followed by continuous injection of prodrug 5-fluorocytosine (5FC) when compared with mice treated with control adenovirus AdlacZ/5FC, AdCD/5FC or AdGMCSF alone ($P < 0.01$). After combined therapy the expression of MHC-I (H-2Db) and B7-1 molecules on freshly isolated tumor cells increased greatly and more dendritic cells and CD8+ T cells infiltrated into the tumor mass. The activity of specific cytotoxic T lymphocytes was also found to be induced more significantly after the combined therapy. Further experiments showed that apoptosis of tumor cells and induction of antitumor immune response might be involved in the mechanisms of the tumor cell killing by the combined therapy. Our results demonstrated that combined transfer of the GM-CSF and CD suicide genes, being able to inhibit the growth of melanoma synergistically and induce specific antitumor immune response efficiently, thus addressing the drawbacks of suicide gene therapy or cytokine gene therapy which were proved to be not satisfactory when used alone, might be of therapeutic potential for gene therapy of cancer.

L27 ANSWER 5 OF 36 CANCERLIT

DUPLICATE 7

ACCESSION NUMBER: 97013727 CANCERLIT
DOCUMENT NUMBER: 97013727
TITLE: Enhanced efficacy of combination of IL-2 gene and IL-6 gene-transfected tumor cells in the treatment of established metastatic tumors.
AUTHOR: Cao X; Chen C; Zhang W; Tao Q; Yu Y; Ye T
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, PR China.
SOURCE: GENE THERAPY, (1996). Vol. 3, No. 5, pp. 421-6.
Journal code: CCE. ISSN: 0969-7128.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 97013727
ENTRY MONTH: 199706

AB IL-2 and IL-6 are important cytokines which have potent antitumor effects and can cooperate to induce immune responses more effectively. IL-2 gene or IL-6 gene-transfected tumor cells exhibited reduced tumorigenicity and decreased metastatic potential. In order to increase the therapeutic efficacy of IL-2 gene-, IL-6 gene-modified tumor vaccines, the experimental pulmonary metastatic melanoma-bearing mice were treated with inactivated IL-2 gene-transfected tumor cells and inactivated IL-6

gene-transfected tumor cells. After the combined vaccination, the pulmonary metastases were reduced more significantly and the survival time of tumor-bearing mice was also markedly prolonged. The CTL activity, NK activity and IL-2-induced LAK activity, IL-2 and TNF secretion from the splenocytes of the above tumor-bearing mice increased more significantly than that of tumor-bearing mice vaccinated with IL-2 gene-transfected vaccine or IL-6 gene transfected vaccine alone. These results demonstrated that the combined use of IL-2 gene-transfected tumor vaccine and IL-6 gene-transfected tumor vaccine could achieve more potent antitumor effect via more effective activation of specific and non-specific antitumor immune responses.

L27 ANSWER 6 OF 36 CANCERLIT
ACCESSION NUMBER: 96101912 CANCERLIT
DOCUMENT NUMBER: 96101912
TITLE: Induction of antitumor immunity and treatment of preestablished tumor by interleukin-6-gene-transfected melanoma cells combined with low-dose interleukin-2.
AUTHOR: Cao X; Zhang W; Gu S; Yu Y; Tao Q; Ye T
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, China.
SOURCE: JOURNAL OF CANCER RESEARCH AND CLINICAL ONCOLOGY, (1995). Vol. 121, No. 12, pp. 721-8.
Journal code: HL5. ISSN: 0171-5216.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: MEDL; L; Priority Journals; Cancer Journals
LANGUAGE: English
OTHER SOURCE: MEDLINE 96101912
ENTRY MONTH: 199602
AB Transfer of cytokine genes into tumor cells has proven a valuable approach for cancer treatment. In order to generate a more effective cancer vaccine, we transfected the human interleukin-6 (IL-6) gene into B16 melanoma cells. A B16 cell clone secreting the highest level of IL-6 was obtained by G418-resistant selection, limiting dilution and IL-6 assay. The IL-6-gene-transfected tumor cells exhibited in vitro growth inhibition, reduced tumorigenicity and decreased metastatic competence. After immunization with the inactivated IL-6-gene-transfected vaccine, the murine cytotoxic T lymphocyte activity, natural killer activity and lymphokine-activated killer activity increased markedly. After treatment with the vaccine, the tumor-bearing mice showed significant growth inhibition of subcutaneous tumor, reduction in pulmonary metastases and extension of survival time. The above therapeutic effect was better when low-dose IL-2 was administered simultaneously, although this dosage of IL-2 had no in vivo antitumor effect. These data demonstrated that IL-6-gene-transfected cancer vaccine has a potent antitumor effect via efficient induction of antitumor immunity, and a better therapeutic effect could be achieved when the vaccine is combined with low-dose IL-2 as adjuvant.

L27 ANSWER 7 OF 36 CANCERLIT
ACCESSION NUMBER: 96287022 CANCERLIT
DOCUMENT NUMBER: 96287022
TITLE: Antitumor effect of interleukin-2 gene-transfected tumor vaccine in combination with interleukin-6 gene-transfected tumor vaccine.
AUTHOR: Cao X; Zhang W; Tao Q
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai.
SOURCE: CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (1995). Vol. 75, No. 10 602-5, pp. 639.
Journal code: CDG. ISSN: 0376-2491.
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: MEDL; L
LANGUAGE: Chinese
OTHER SOURCE: MEDLINE 96287022
ENTRY MONTH: 199610

AB It has been shown that IL-2 and IL-6 can cooperate to induce immune responses more effectively. In order to increase the therapeutic efficacy of cytokine gene-transfected tumor vaccines, we treated the experimental pulmonary metastatic melanoma-bearing mice with IL-2 gene-transfected tumor vaccine and IL-6 gene-transfected tumor vaccine. After the combined treatment, the pulmonary metastases were reduced more significantly and the survival time of tumor-bearing mice was also prolonged more significantly. The CTL activity, NK activity and IL-2-induced LAK activity, IL-2 and TNF secretion from the splenocytes of the above tumor-bearing mice increased more significantly than that of tumor-bearing mice treated with IL-2 gene-transfected vaccine or IL-6 gene-transfected vaccine alone. These results demonstrated that the combined use of IL-2 gene-transfected tumor vaccine and IL-6 gene-transfected tumor vaccine could achieve more potent antitumor effect via more efficient activation of immune functions. The experiment outlines a novel approach to the cytokine gene therapy of cancer.

L27 ANSWER 8 OF 36 CANCERLIT

ACCESSION NUMBER: 96147754 CANCERLIT

DOCUMENT NUMBER: 96147754

TITLE: Enhanced immune functions and antitumor activity of fibroblast-mediated interleukin-2 gene therapy.

AUTHOR: Cao X T; Zhang W P; Tao Q

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai.

SOURCE: CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (1995). Vol. 75, No. 9 521-4, pp. 573.

Journal code: CDG. ISSN: 0376-2491.

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

FILE SEGMENT: MEDL; L

LANGUAGE: Chinese

OTHER SOURCE: MEDLINE 96147754

ENTRY MONTH: 199604

AB The aim of the present study was to establish fibroblastmediated IL-2 gene therapy and to observe its antitumor effect in the mouse tumor model. The IL-2 gene-transfected fibroblasts (NIH3T3-IL-2+) secreting high level of IL-2 were encapsulated with collagen and then implanted i.p. into mice. Certain level of IL-2 could be detected in murine serum for some periods, and the splenic proliferation, NK and LAK activities, cytokine production (IFN- γ , TNF, IL-2) were enhanced significantly. It was of great importance that the high endogenous LAK activity was induced. The significant therapeutic effect of i.p. implantation of NIH3T3-IL-2+ on ascitic liver carcinoma-bearing mice was observed. The better therapeutic results could be achieved. NIH3T3-IL-2+ cells were i.p. implanted in combination with i.p. injection of LAK cells. These results demonstrated that fibroblast--mediated IL-2 gene therapy has potent antitumor effect via augmentation of immune functions and the antitumor effect will be more obvious when IL-2 gene therapy is used along with the adoptive transfer of LAK cells.

L27 ANSWER 9 OF 36 MEDLINE

ACCESSION NUMBER: 2002047845 MEDLINE

DOCUMENT NUMBER: 21631640 PubMed ID: 11775265

TITLE: Macrophage activation of lymphoma-bearing mice by liposome-mediated intraperitoneal IL-2 and IL-6 gene therapy.

AUTHOR: Wang Q; Cao X; Wang J; Zhang W; Tao Q; Ye T

CORPORATE SOURCE: Department of Immunology, Second Military Medical

SOURCE: University, Shanghai 200433, China.
CHINESE MEDICAL JOURNAL, (2000 Mar) 113 (3) 281-5.
Journal code: 7513795. ISSN: 0366-6999.

PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200202

ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020208
Entered Medline: 20020207

AB OBJECTIVE: To investigate the antitumor mechanism of interleukin-2 (IL-2) and interleukin-6 (IL-6) gene therapy. METHODS: Liposome encapsulated IL-2 DNA and IL-6 DNA were intraperitoneally (i.p.) injected into mouse lymphoma cell line (EL-4) lymphoma-bearing mice. Macrophage function (M phi) from the mice was assessed. RESULTS: Cytotoxicity, major histocompatibility (MHC) II expression and IL-1 and TNF secretion of the macrophages all augmented after i.p. injection of liposome encapsulated IL-2 DNA or IL-6 DNA. More efficient activation of macrophages was observed in mice treated with liposome encapsulated IL-2 DNA than IL-6 DNA. IL-2 gene therapy combined with IL-6 gene therapy showed the maximal activation of macrophages in the lymphoma-bearing mice. CONCLUSION: IL-2 and IL-6 gene therapy can relieve the suppression of macrophages of the lymphoma-bearing mice, and efficiently activate the antitumor immune responses.

L27 ANSWER 10 OF 36 MEDLINE DUPLICATE 9

ACCESSION NUMBER: 96287022 MEDLINE

DOCUMENT NUMBER: 96287022 PubMed ID: 8697075

TITLE: Antitumor effect of interleukin-2 gene-transfected tumor vaccine in combination with interleukin-6 gene-transfected tumor vaccine.

AUTHOR: Cao X; Zhang W; Tao Q

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai.

SOURCE: CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (1995 Oct) 75 (10) 602-5, 639.
Journal code: CDG; 7511141. ISSN: 0376-2491.

PUB. COUNTRY: China
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: Chinese

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199609

ENTRY DATE: Entered STN: 19960912
Last Updated on STN: 19970203
Entered Medline: 19960903

AB It has been shown that IL-2 and IL-6 can cooperate to induce immune responses more effectively. In order to increase the therapeutic efficacy of cytokine gene-transfected tumor vaccines, we treated the experimental pulmonary metastatic melanoma-bearing mice with IL-2 gene-transfected tumor vaccine and IL-6 gene-transfected tumor vaccine. After the combined treatment, the pulmonary metastases were reduced more significantly and the survival time of tumor-bearing mice was also prolonged more significantly. The CTL activity, NK activity and IL-2-induced LAK activity, IL-2 and TNF secretion from the splenocytes of the above tumor-bearing mice increased more significantly than that of tumor-bearing mice treated with IL-2 gene-transfected vaccine or IL-6 gene-transfected vaccine alone. These results demonstrated that the combined use of IL-2 gene-transfected tumor vaccine and IL-6 gene-transfected tumor vaccine could achieve more potent antitumor effect via more efficient activation of immune functions. The experiment outlines a novel approach to the cytokine gene therapy of cancer.

L27 ANSWER 11 OF 36 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 96147754 MEDLINE
DOCUMENT NUMBER: 96147754 PubMed ID: 8556540
TITLE: Enhanced immune functions and antitumor activity of fibroblast-mediated interleukin-2 gene therapy.
AUTHOR: Cao X T; Zhang W P; Tao Q
CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai.
SOURCE: CHUNG-HUA I HSUEH TSA CHIH [CHINESE MEDICAL JOURNAL], (1995 Sep) 75 (9) 521-4, 573.
PUB. COUNTRY: China
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: Chinese
ENTRY MONTH: Priority Journals
ENTRY DATE: 199602
Entered STN: 19960312
Last Updated on STN: 19970203
Entered Medline: 19960223

AB The aim of the present study was to establish fibroblast-mediated IL-2 gene therapy and to observe its antitumor effect in the mouse tumor model. The IL-2 gene-transfected fibroblasts (NIH3T3-IL-2+) secreting high level of IL-2 were encapsulated with collagen and then implanted i.p. into mice. Certain level of IL-2 could be detected in murine serum for some periods, and the splenic proliferation, NK and LAK activities, cytokine production (IFN- γ , TNF, IL-2) were enhanced significantly. It was of great importance that the high endogenous LAK activity was induced. The significant therapeutic effect of i.p. implantation of NIH3T3-IL-2+ on ascitic liver carcinoma-bearing mice was observed. The better therapeutic results could be achieved. NIH3T3-IL-2+ cells were i.p. implanted in combination with i.p. injection of LAK cells. These results demonstrated that fibroblast-mediated IL-2 gene therapy has potent antitumor effect via augmentation of immune functions and the antitumor effect will be more obvious when IL-2 gene therapy is used along with the adoptive transfer of LAK cells.

L27 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 6
ACCESSION NUMBER: 1997:643899 CAPLUS
DOCUMENT NUMBER: 127:317930
TITLE: In vivo distribution and gene expression of genetically modified hepatocytes after intrasplenic transplantation
AUTHOR(S): Zhang, Weiping; Cao, Xuetao; Huang, Xin; Wang, Jianli; Tao, Qun; Ye, Tianxing
CORPORATE SOURCE: Dep. Immunol., Second Military Med. Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Sci. China, Ser. C: Life Sci. (1997), 40(5), 554-560
PUBLISHER: CODEN: SCCLFO; ISSN: 1006-9305
DOCUMENT TYPE: Science in China Press
LANGUAGE: Journal
English

AB To investigate the feasibility and efficacy of liver gene therapy mediated by intrasplenic transplantation of genetically modified hepatocytes, the normal mouse liver cell line BNL CL.2 cells were introduced with Neo-resistant (NeoR) gene or interleukin-2 (IL-2) gene in vitro, and transplanted intrasplenically into normal syngeneic mice (2.times.10⁶ cell/mouse); subsequently, the expressions of the introduced genes in vivo were detected. The RT-PCR results showed that NeoR mRNA expressions were detectable in livers 24 h after transplantation and lasted over 11 wk. Moreover, the NeoR mRNA was detected to be expressed temporarily in spleens (24 h-1 wk) and lungs (24-96 h) after transplantation. After intrasplenic transplantation of IL-2 gene-modified BNL CL.2 cells, the

stable expression of IL-2 mRNA in the livers of transplanted mice was detectable by RT-PCR (24 h-11 wk), and certain levels of IL-2 (5-40 pg/mL) remained in the peripheral blood. When IL-2 gene-modified BNL CL.2 cells were transplanted intrasplenically to treat the metastatic liver colon carcinoma-bearing mice, the survival time of the treated mice was significantly prolonged. The data indicate that intrasplenic transplantation of genetically modified hepatocytes could allow for distribution in host livers and long-term survival of the transplanted liver cells, and effective expression of exogenous genes in vivo, suggesting that this can be a candidate approach to liver-directed gene therapy.

L27 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:22530 CAPLUS

DOCUMENT NUMBER: 136:80886

TITLE: Human interferon-like protein and its cDNA and therapeutic use thereof

INVENTOR(S): Cao, Xuetao; Zhang, Weiping; Wan, Tao; Chen, Guoyou; Tao, Qun; Ju, Dianwen; Lei, Hong

PATENT ASSIGNEE(S): Shanghai Huachen Biological Technology Inst., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 23 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| | ----- | ---- | ----- | ----- | ----- |
| AB | CN 1299831 | A | 20010620 | CN 1999-124272 | 19991216 |
| | The invention provides cDNA sequences of a novel human interferon-like protein (named as IFL) cloned from human dendritic cell. The invention also relates to constructing the cloned gene expression vectors to prep. its recombinant protein using E. coli cells or eukaryotic cells. Methods of expressing and prepg. the above recombinant protein and its antibody are described. Methods of using related gene or protein products for the treatment of various kinds of diseases, such as cancer, viral infection, and immune diseases are also disclosed. Methods for screening for related analogs, agonists, inhibitors and antagonists to be used as therapeutic drugs are also described. | | | | |

L27 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:148998 CAPLUS

DOCUMENT NUMBER: 136:162352

TITLE: Protein and cDNA sequences of human cytokine receptor-like protein 1 and therapeutic use thereof

INVENTOR(S): Cao, Xuetao; Zhang, Weiping; He, Long; Wan, Tao; Li, Nan; Yuan, Zhenglong; Tao, Qun

PATENT ASSIGNEE(S): Shanghai Huachen Biological Technology Inst., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 27 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------------|------|----------|-----------------|----------|
| | ----- | ---- | ----- | ----- | ----- |
| | CN 1299828 | A | 20010620 | CN 1999-124269 | 19991216 |

AB The invention provides protein and cDNA sequences for novel human protein CRL1 cloned from dendritic cell, and which has sequence homol. with known gp130 receptor. The invention also relates to constructing CRL1 gene expression vectors to prep. recombinant CRL1 using prokaryote or eukaryote cells. Methods of expressing and prep. recombinant CRL1 and its antibody are described. Methods of using CRL1 or genes for the treatment of various kinds of diseases, such as cancer, transplant rejection and inflammation are also disclosed.

L27 ANSWER 15 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:6828 CAPLUS

DOCUMENT NUMBER: 136:97320

TITLE: cDNA and protein sequence of interleukin 17 sequence homolog CX1 from human and their uses

INVENTOR(S): **Zhang, Weiping; Cao, Xuetao;** Chen, Guoyou; Wan, Tao; Ju, Dianwen; **Tao, Qun;** Lei, Hong

PATENT ASSIGNEE(S): Shanghai Huachen Biological Technology Inst., Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 31 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| CN 1299823 | A | 20010620 | CN 1999-124235 | 19991210 |

AB This invention provides the cDNA and protein sequence of novel human interleukin 17 sequence homolog CX1. The CX1 consists of 180 amino acids with 20 amino acid long signal peptide at N-terminal. The protein sequence of CX1 has high homol. with that of human interleukin 17. The invention also provides the tissue distribution of CX1 gene and the process of expression of CX1 in animal cell line TF-1 stimulating the proliferation of the cell.

L27 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:266754 CAPLUS

DOCUMENT NUMBER: 134:261855

TITLE: Method for constructing adenoviral vector expressing human interleukin 12 and therapeutic uses thereof

INVENTOR(S): **Cao, Xuetao; Zhang, Weiping;** Ju, Dianwen; **Tao, Qun**

PATENT ASSIGNEE(S): Huachen Inst. of Biological Technology, Shanghai, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 27 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| CN 1258740 | A | 20000705 | CN 1998-126748 | 19981231 |

AB The invention provides a method for constructing human interleukin 12 (IL-12) expression cassette Ad-hIL-12 (CCTCC No. V98006) using human adenovirus (Ad5) with two deletions of E1 region and E3 region of genomic DNA, and two terminal peptides (TP) at both-sides of Ad5 genomic DNA, and human IL-12 cDNA inserted in the E1 deletion region. The human IL-12 expression cassette contains promoter (giant cell virus promoter or bovine papilloma virus promoter), coding sequences of IL-12 subunits, p35 and

p40, poly(A) signal, terminator, and internal ribosome binding site between p35 and p40 subunits. The invention further relates to the therapeutic uses of human interleukin 12 (IL-12) expression cassette.

L27 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:279712 CAPLUS
DOCUMENT NUMBER: 134:279579
TITLE: Recombinant adenovirus vector expressing human interleukin 18, its preparation and use
INVENTOR(S): Cao, Xuetao; Zhang, Weiping; He, Long; Ju, Dianwen; Tao, Qun
PATENT ASSIGNEE(S): Huachen Inst. of Biological Technology, Shanghai, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 27 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| CN 1258739 | A | 20000705 | CN 1998-126747 | 19981231 |

AB The invention also relates to constructing adenovirus vector to produce recombinant interleukin 18 (IL-18), which can be used in gene therapy. The recombinant adenovirus used for vector prepn. is type 5 adenovirus with E1 and E3 regions deleted and the cDNA for IL-18 is inserted into E1 gene. IL-18 gene includes signal peptide coding region and is under the control of a promoter for Cytomegalovirus, or bovine papilloma virus. The IL-18 signal peptide can be selected from cellular factors, or IL-1 receptor, transmembrane proteins, chemokines, or growth factors. One recombinant adenovirus (Ad5) Ad-hIL-18 is prepd. by cotransfecting 293 cell with linear Ad5 DNA with two terminal peptides (TP) attached to its ends and IL-18 vectors.

L27 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:279711 CAPLUS
DOCUMENT NUMBER: 134:276169
TITLE: Recombinant adenovirus vector expressing human granulocyte-macrophage colony-stimulating factor, its preparation and use
INVENTOR(S): Cao, Xuetao; Zhang, Weiping; Tao, Qun; Ju, Dianwen
PATENT ASSIGNEE(S): Huachen Inst. of Biological Technology, Shanghai, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 24 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| CN 1258738 | A | 20000705 | CN 1998-126746 | 19981231 |

AB The invention also relates to constructing adenovirus vector to produce recombinant granulocyte-macrophage colony-stimulating factor (GM-CSF), which can be used in gene therapy. The recombinant adenovirus used for vector prepn. is type 5 adenovirus with E1 and E3 regions deleted and the cDNA for GM-CSF is inserted into E1 gene. GM-CSF gene includes signal peptide coding region and is under the control of a promoter for Cytomegalovirus, or bovine papilloma virus. The GM-CSF signal peptide can be selected from cellular factors, or IL-1 receptor, transmembrane

proteins, chemokines, or growth factors. One recombinant adenovirus Ad-hGM-CSF is prepd. by cotransfecting 293 cell with linear Ad5 DNA with two terminal peptides (TP) attached to its ends and GM-CSF vectors.

L27 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:433500 CAPLUS

DOCUMENT NUMBER: 133:84757

TITLE: Preparation of human GM-CSF using genetically engineered Escherichia coli

INVENTOR(S): Cao, Xuetao; Tao, Qun; Zhang, Weiping; Ju, Dianwen

PATENT ASSIGNEE(S): Huachen Biotechnology Inst., Shanghai, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 22 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| | ----- | ---- | ----- | ----- | ----- |
| AB | CN 1228476 | A | 19990915 | CN 1998-106057 | 19980305 |
| | The human GM-CSF (granulocyte macrophage colony stimulating factor) secretion expression vector, pHuGM-CSF, is constructed by putting coding sequences for E. coli heat-stable enterotoxin II (STII) signal peptide and human GM-CSF fusion protein under the control of the promoter of E. coli alk. phosphatase gene phoA. The cDNA of human GM-CSF is amplified by RT-PCR from human peripheral blood mononuclear cells. The bacterial expression host is E. coli transformed with the secretion vector pHuGM-CSF -- W3110/pHuGM-CSF. Methods of expression and purifn. of the recombinant GM-CSF using the transformed bacteria is provided and the purified GM-CSF protein (with STII signal peptide cleaved and Ala at the N-terminus) is analyzed by SDS-PAGE. | | | | |

L27 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:433499 CAPLUS

DOCUMENT NUMBER: 133:88236

TITLE: Preparation of human interleukin-2 (IL-2) using genetically engineered Escherichia coli

INVENTOR(S): Cao, Xuetao; Tao, Qun; Zhang, Weiping; Ju, Dianwen

PATENT ASSIGNEE(S): Huachen Biotechnology Inst., Shanghai, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 19 pp. CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| | ----- | ---- | ----- | ----- | ----- |
| AB | CN 1228475 | A | 19990915 | CN 1998-105441 | 19980306 |
| | The human IL-2 expressing vector pBV-125Ser-rhIL-2 is constructed by inserting its cDNA into plasmid pBV220. The IL-2 cDNA is amplified from human peripheral blood mononuclear cells by PCR and the codon for Cys125 has been mutated to Ser to increase the protein stability. The host cell, E. coli DH5.alpha./pBV-125Ser-rhIL-2, is generated by transformation, and the recombinant human IL-2 (rhIL-2) is expressed in the inclusion body inside the bacteria. Methods of isolating bacterial inclusion bodies and purifn. of rhIL-2 is provided. The purified IL-2 is analyzed by SDS-PAGE and sequenced up to 15 N-terminal amino acid residues for the | | | | |

confirmation. The specific activity of these purified IL-2 is 3.0x107U/mg.

L27 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:358862 CAPLUS

DOCUMENT NUMBER: 131:140134

TITLE: Therapeutic effect of combined treatment with cytosine deaminase suicide gene and GM-CSF gene on murine melanoma and its immunological mechanism

AUTHOR(S): Ju, Dianwen; **Cao, Xuetao**; Wang, Baomei; Yin, Pingzhang; Wan, Tao; **Tao, Qun**; **Zhang, Weiping**

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Zhonghua Weishengwuxue He Mianyixue Zazhi (1999), 19(2), 148-151

CODEN: ZWMZDP; ISSN: 0254-5101

PUBLISHER: Weishenbu Beijing Shengwu Zhipin Yanjiuso

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Objective: To observe the therapeutic effect of adenovirus expressing cytosine deaminase (AdCD) in combination with adenovirus expressing GM-CSF (AdGMCSF) followed by administration of a kind of prodrug, 5 fluorocytosine (5FC) on melanoma in mice. Methods: Melanoma-bearing mice were administered with AdCD/5FC/AdGMCSF, AdCD/5FC, AdGM-CSF, control adenovirus AdlacZ/5FC, or PBS. Results: The results demonstrated that significant growth inhibition of established tumors and prolongation of survival period were obsd. in tumor-bearing mice after AdCD/5FC/AdGMCSF combined therapy when compared with mice treated with AdCD/5FC, AdGM-CSF, AdlacZ/5FC, or PBS. The activity of cytotoxic T lymphocytes could be induced after the combined therapy. The expression of MHC-I and B7-1 mols. on freshly isolated tumor cells after combined therapy increased greatly, and more dendritic cells and CD8+ T cells infiltrated into the tumor mass when measured with FACS. Conclusion: combined therapy with suicide gene and GM-CSF gene transfer could directly eradicate established tumors and efficiently induce the antitumor immunity of the mice.

L27 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:629211 CAPLUS

DOCUMENT NUMBER: 130:76670

TITLE: Therapeutic effects of combined suicide gene and cytokine gene therapy on erythroleukemia-bearing mice

AUTHOR(S): Ju, Dianwen; **Cao, Xuetao**; Wang, Baomei; Kong, Lingfei; Yin, Pingzhang; Wan, Tao; **Tao, Qun**; **Zhang, Weiping**

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Zhonghua Xueyexue Zazhi (1998), 19(6), 294-298

CODEN: CHTCD7; ISSN: 0253-2727

PUBLISHER: Zhongguo Yixue Kexueyuan Xueyexue Yanjiuso

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Adenovirus harboring E. coli, cytosine deaminase (CD) suicide gene and/or GM-CSF gene (Ad-GM-CSF) were used for the treatment of erythroleukemia-bearing mice to explore the antitumor effect of combined transfer of suicide gene and GM-CSF gene in erythroleukemia-bearing mice. The mice were inoculated with FBL-3 erythroleukemia cells s.c. and received Ad-CD followed by 5-fluorocytosine treatment with or without Ad-GM-CSF 3 days later. The mice received Ad-CD/5FC and Ad-GM-CSF developed tumors more slowly and survived much longer than those received Ad-CD/5FC alone, Ad-GM-CSF alone, control virus Ad-LacZ/5FC or PBS. Combined transfer of CD gene and GM-CSF gene induced a higher specific CTL activity than control therapies did. There were tumor necrosis and

massive lymphocyte infiltration in the mice after the combined therapy. Combined transfer of suicide gene and cytokine gene could synergistically inhibit the growth of erythroleukemia cells in the mice and induce tumor specific immunity of the host.

L27 ANSWER 23 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:459293 CAPLUS

DOCUMENT NUMBER: 129:239529

TITLE: Antitumor effect of combined therapy with adenovirus mediated CD suicide gene and interleukin 2 gene transfer and its immunological mechanism

AUTHOR(S): Ju, Dianwen; **Cao, Xuetao**; Wang, Baomei; Wan, Tao; **Tao, Qun**; Chen, Guoyou; **Zhang, Weiping**

CORPORATE SOURCE: Department of Immunology, 2nd Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Zhonghua Zhongliu Zazhi (1998), 20(2), 108-111

PUBLISHER: CODEN: CCLCDY; ISSN: 0253-3766

DOCUMENT TYPE: Zhongguo Yixue Kexueyuan Zhongliu Yanjiuso

LANGUAGE: Journal

Chinese

AB Adenovirus harboring E. coli cytosine deaminase gene (AdCD) and/or IL-2 gene (AdIL-2) local injection were used in treatment of B16F10 melanoma cell bearing mice followed by i.p. injection of 5- fluorocytosine (5-Fc) 30 mg/kd/d for 10 days. The AdIL-2/5-Fc or AdCD/5-Fc treated mice had inhibited tumor growth and prolonged survival vs. the control AdlacZ/5-Fc and PBS mice, $P < 0.05$. The inhibition of tumor growth and prolonged survival were even more evident in AdCD+AdIL-2/5-Fc treated mice, $P < 0.05$, and 6/10 mice were survived with the tumor mass disappeared. The treated mice were found to induce enhanced splenocyte nature killer and specific cytotoxic T cell activity, and increased tumor CD4++ and CD8+ T cell infiltration. FACS anal. demonstrated that the therapy increased the expression of H-2K+b and B7-1 on freshly isolated tumor cells. The results suggest that transfer of CD suicide gene plus 5-Fc combined with transfer of IL-2 gene synergistically inhibit the growth of melanoma cells in mice; beside the cytotoxic effect of 5- Fc, specific and non-specific antitumor immunity are responsible.

L27 ANSWER 24 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:170122 CAPLUS

DOCUMENT NUMBER: 131:4055

TITLE: Induction of immune response by IL-6 gene-modified leukemia cells

AUTHOR(S): **Cao, Xuetao**; Ge, Lingfu; Ju, Dian Wen; Yu, Yizhi; **Tao, Qun**; **Zhang, Weiping**

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Chin. J. Cancer Res. (1998), 10(1), 9-15

PUBLISHER: CODEN: CJCRFH; ISSN: 1000-9604

DOCUMENT TYPE: Chinese Journal of Cancer Research

LANGUAGE: Journal

English

AB Human IL-6 gene was transduced into FBL-3 murine erythroleukemia cells in vitro by calcium phosphate co-pptn. After selection in the presence of G418, limiting diln. and biol. activity assay, G418 resistant clone that secreted the highest level of IL-6 (225.6 U/mL) was selected out of 24 IL-6-secreting clones. The FBL-3 cells secreting the highest level of IL-6 (FBL-3-IL-6) showed decreased growth potential and clonogenicity in vitro. Inhibition of cell growth and clone formation was closely related to the level of IL-6 secretion. FBL-3-IL-6 cells grew more slowly than wild-type FBL-3 leukemia cells and FBL-3 cells secreting lower level of IL-6 (21.3 U/mL) when inoculated s.c. into C57BL/6 mice. The mice inoculated with FBL-3-IL-6 cells showed prolonged survival period than

those inoculated with control leukemia cells. Increased cytotoxic activities of splenic NK and CTL were found in mice inoculated with FBL-3-IL-6 cells. The secretions of IL-2, TNF and GM-CSF from murine splenocytes were also greatly elevated after the inoculation of FBL-3-IL-6 leukemia cells. These data suggested that transduction of IL-6 gene into FBL-3 cells decreased the tumorigenicity and increased the immunogenicity of the leukemia cells, could induce specific and nonspecific antitumor immune responses. IL-6 gene-modified leukemia cells might be of great interests to be used as vaccine for the treatment of leukemia.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:261494 CAPLUS

DOCUMENT NUMBER: 129:94114

TITLE: Anti-tumor effect of oncolyzate from melanoma transfected with granulocyte-macrophage colony stimulating factor gene-encoded vaccinia virus

AUTHOR(S): Ju, Dianwen; Cao, Xuetao; Wan, Tao;

Tao, Qun; Yu, Yizhi; Zhang, Weiping

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Zhonghua Weishengwuxue He Mianyixue Zazhi (1997), 17(5), 382-386

CODEN: ZWMZDP; ISSN: 0254-5101

PUBLISHER: Weishenbu Beijing Shengwu Zhipin Yanjiuso

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Recombinant vaccinia virus harboring murine granulocyte macrophage colony-stimulating factor (GM-CSF) gene was constructed to prep. vaccinia melanoma oncolyzate (VMO). VMO prepd. with vaccinia virus infected B16-F10 cells were tested for its therapeutic effect on the growth of s.c. melanoma. C57BL/6 mice were inoculated with 1×10^5 B16-F10 melanoma cells s.c. and VMO infected with GM-CSF gene encoded vaccinia virus (GM-CSFVMO) and thymidine kinase gene deficient vaccinia virus (TKVMO) or B16-F10 melanoma oncolyzate (BMO), were injected at the site of tumor inoculation 3 days later. The same therapy were bolstered 1 wk later. The GM-CSFVMO treatment significantly inhibited the growth of s.c. tumor and prolonged the survival period of tumor-bearing mice. Immunization with GM-CSFVMO could elicit strong antitumor cellular immunity and delay the time of tumor formation when re-challenged by wild type B16-F10 cells. Further study elucidated that cytotoxicity of PBL and lymphocytes in spleen towards B16-F10 was obviously increased after treatment or immunization with GM-CSFVMO. These results suggest that the tumor oncolyzate vaccine prepd. with GM-CSF gene-encoded vaccinia virus may exert potent therapeutic effect through the efficient induction of antitumor immunity of the host.

L27 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:170171 CAPLUS

DOCUMENT NUMBER: 131:54444

TITLE: Construction and expression of the replication-deficient adenovirus vector of human GM-CSF

AUTHOR(S): Zhang, Weiping; Cao, Xuetao;

Tao, Qun; Hamada, Hirofumi

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Chin. J. Cancer Res. (1997), 9(4), 304-308

CODEN: CJCRFH; ISSN: 1000-9604

PUBLISHER: Chinese Journal of Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The full-length cDNA encoding human granulocyte-macrophage colony-stimulating factor (GM-CSF) was cloned by RT-PCR, placed under the control of CMV promoter, and inserted into adenovirus vector of E1-substitution type, pAxlw. Subsequently, the cassette cosmid was cotransfected into 293 cells together with EcoT22I-digested Ad5-TPC, and the replication-deficient recombinant adenoviruses (Ad) of human GM-CSF were generated efficiently by homologous recombination, with the titers of 1.51.times.10⁹pfu/mL. 48 H after infection with prepd. human GM-CSF recombinant adenoviruses in vitro, HeLa cells and primary human skin fibroblasts expressed high levels of human GM-CSF (80.apprx.400ng/106cells/24h). These suggest that the recombinant Ad of human GM-CSF prepd. by COS/TPC method is effective in mediating GM-CSF gene transfer and might be used in cancer gene therapy.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:170162 CAPLUS

DOCUMENT NUMBER: 131:4063

TITLE: Antitumor effect of granulocyte-macrophage colony-stimulating factor (GM-CSF)-gene encoded vaccinia melanoma oncolyzate and its immunological mechanisms

AUTHOR(S): Ju, Dian Wen; Cao, Xuetao; Wan, Tao; Zhang, Weiping; Tao, Qun; Yu, Yizhi; Chen, Guoyou

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Chin. J. Cancer Res. (1997), 9(4), 263-267

CODEN: CJCRFH; ISSN: 1000-9604

PUBLISHER: Chinese Journal of Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vaccinia melanoma oncolyzate (VMO) prepd. by infecting B16F10 melanoma cells with recombinant vaccinia virus encoding murine GM-CSF gene was tested for its therapeutic effect on the preestablished melanoma. C57BL/6 mice were inoculated s.c. with 1.times.10⁵ B16F10 melanoma cells and received s.c. administration with VMO prepd. with GM-CSF gene-encoded vaccinia virus(GM-CSFVMO), VMO prepd. with thymidine kinase gene-deficient vaccinia virus(TKVMO), B16F10 melanoma oncolyzate(BMO), or PBS 3 days after tumor inoculation. The same treatment was bolstered one week later. The results demonstrated that GM-CSFVMO treatment significantly inhibited the growth of s.c. tumor and prolonged the survival period of tumor-bearing mice. Further study elucidated that cytotoxicity of PBL and splenocytes towards B16F10 increased obviously after treatment with GM-CSFVMO, but NK activity remained unchanged. These results suggest that the tumor oncolyzate vaccine prepd. with GM-CSF gene-encoded vaccinia virus might exert potent therapeutic effect on the preestablished tumor through the efficient induction of specific antitumor immune response of the host.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:385938 CAPLUS

DOCUMENT NUMBER: 129:183896

TITLE: In vivo gene therapy of murine melanoma mediated by local transfection of recombinant vaccinia virus encoding human interleukin-2

AUTHOR(S): Wan, Tao; Cao, Xuetao; Liu, Jiangqiu; Ju, Dianwen; Tao, Qun; Chen, Guoyou; Zhang, Weiping; Yu, Yizhi

CORPORATE SOURCE: Department of Immunology, Second Military Medical

SOURCE: University, Shanghai, 200433, Peop. Rep. China
Zhongguo Mianyixue Zazhi (1997), 13(4), 211-214
CODEN: ZMZAEE; ISSN: 1000-484X
PUBLISHER: Zhongguo Mianyixue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Murine melanoma was treated by local transfection of recombinant vaccinia virus encoding human interleukin-2 (rVV-IL-2). In vivo rVV-IL-2 transfection resulted in inhibition of tumor growth and prolonged the survival time of tumor-bearing mice. The splenocytes from rVV-IL-2 treated mice had higher cytotoxicity of NK, LAK and CTL than the controls. The in vivo transfection mediated by rVV-IL-2 was potentially feasible for the cancer gene therapy.

L27 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:543033 CAPLUS
DOCUMENT NUMBER: 125:193160
TITLE: Increased expression of ICAM-1 glycoprotein in B16 melanoma cells transfected with interleukin (IL)-2 gene and IL-4 gene
AUTHOR(S): Chen, Guoyou; Cao, Xuetao; Yu, Yizhi;
Zhang, Weiping; Tao, Qun
CORPORATE SOURCE: Dep. Immunol., Second Military Med. Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Mianyixue Zazhi (1996), 12(1), 20-24
CODEN: ZMZAEE; ISSN: 1000-484X
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Interleukin (IL)-2 gene and IL-4 gene were transfected into B16 melanoma cells, and their tumorigenicity were then studied in vivo. The expression level of ICAM-1 were also detected by the FACS method. Sensitivities of the cytokine gene transfected B16 cells to LAK, CTL cytotoxicity were compared with that of the wild-type B16 cells. Both IL-2 gene and IL-4 gene-transfected B16 cells had higher ICAM-1 expression than the wild-type B16 cells. These cytokine genes-modified B16 cells become more sensitive to LAK or CTL (cytotoxic T cell) cytotoxicity, and that higher sensitivity was abolished by anti-ICAM-1 monoclonal antibody. Thus, the decreased tumorigenicity of the IL-2 gene, IL-4 gene transfected B16 melanoma cells can be attribute to not only their increased antitumor immunity of the host, but also to the increased sensitivity to effector cells by increased ICAM-1 expression.

L27 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:272019 CAPLUS
DOCUMENT NUMBER: 124:340647
TITLE: Augmentation of antitumor immunity by interleukin-3 gene transfected melanoma cells
AUTHOR(S): Zhang, Weiping; Cao, Xuetao; Xu, Zhigong; Tao, Qun; Ye, Tianxin
CORPORATE SOURCE: Dep. Immunology, Second Military Medical Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Mianyixue Zazhi (1995), 11(6), 344-7
CODEN: ZMZAEE; ISSN: 1000-484X
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB An interleukin-3 (IL-3) gene transfected murine B16 melanoma cell clone (B16-IL-3) was established, and its tumorigenicity and pulmonary metastatic capability were decreased. The effect of B16-IL-3 cells on the augmentation of antitumor immunity was studied. NK, LAK and CTL cytotoxic activities of splenocytes from B16-IL-3 cell-inoculated C57BL/6 mice were enhanced, and the CD4+ CD8+ ratios increased. The decreased tumorigenicity of B16-IL-3 cells was also found in nu/nu mice.

L27 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:18744 CAPLUS

DOCUMENT NUMBER: 124:53442

TITLE: Decreased tumorigenicity of tumor cells transfected with human interleukin-6 gene

AUTHOR(S): Cao, Xuetao; Zhang, Weiping; Gu, Shen; Tao, Qun; Ye, Tianxing

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Zhonghua Weishengwuxue He Mianyixue Zazhi (1995), 15(2), 135-9

DOCUMENT TYPE: CODEN: ZWMZDP; ISSN: 0254-5101

LANGUAGE: Journal

Chinese

AB To generate a cancer vaccine, the human interleukin-6 (IL-6) gene was transfected into B16 melanoma cells by the calcium phosphate copptn. method. After G418 resistance selection and limiting diln., 21 pos. clones were obtained. A clone named as B16-IL-6+ cells showed in vitro growth inhibition and grew more slowly than wild-type tumor cells after s.c. inoculation. The mice rejecting IL-6-secreting tumor cells exhibited resistance to later challenge with wild-type tumor cells. When injected i.v. in an exptl. metastasis model, B16-IL-6+ cell were inefficient in forming pulmonary metastases and the survival time of tumor-bearing mice was prolonged. Thus, IL-6 gene-transfected tumor cells had decreased tumorigenicity and induced antitumor immunity.

L27 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:718598 CAPLUS

DOCUMENT NUMBER: 123:167048

TITLE: Immunotherapy of cancer by IL-2 gene-transfected tumor vaccine in combination with IL-1, low-dose

AUTHOR(S): cyclophosphamide and its immunological mechanisms

Cao, Xuetao; Zhang, Weiping; Zheng Lingli; Yu, Yizhi; Tao, Qun; Chen, Quoyou; Ye, Tianxing

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China

SOURCE: Zhongguo Mianyixue Zazhi (1994), 10(5), 289-93

DOCUMENT TYPE: CODEN: ZMZAEE; ISSN: 1000-484X

LANGUAGE: Journal

Chinese

AB After treatment with IL-2 gene-transfected vaccine alone, the pulmonary metastases were reduced and the survival time of tumor-bearing mice was prolonged. The anti-metastatic effect was better when the vaccine was used with IL-1 or low-dose Cy. The best therapeutic effect was achieved when IL-2 gene transfected vaccine, IL-1, and low-dose Cy were all used at the same time. The cytotoxicity of murine splenic CTL, NK cells, IL-2 induced LAK cells, and the level of IL-2 and TNF secreted by splenocytes increased after tumor-bearing mice were treated with the vaccine. The above antitumor immune functions were augmented when IL-1 and low-dose Cy were also used. Thus, the vaccine transfected with IL-2 gene had effective anti-metastatic effect through the activation of the in vivo antitumor immunity. When it was used with IL-1 and/or low-dose Cy, the therapeutic effect was better.

L27 ANSWER 33 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:718597 CAPLUS

DOCUMENT NUMBER: 123:167426

TITLE: In vitro and in vivo growth characteristics of a clone of tumor cells transfected with IL-2 gene

AUTHOR(S): Cao, Xuetao; Zhang, Weiping; Zhou, Zhengfang; Zheng, Lingli; Yu, Yizhi; Tao, Qun; Ye, Tianxing

CORPORATE SOURCE: Department of Immunology, Second Military Medical University, Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Mianyixue Zazhi (1994), 10(5), 284-8
CODEN: ZMZAEE; ISSN: 1000-484X
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB To investigate the antitumor effect of tumor vaccine transfected with IL-2 gene which has increased immunogenicity, IL-2 gene-transfected tumor cells which secrete high level of IL-2 must be obtained and the growth characteristics of these tumor cells should be identified. The expression vector BMGNeo-IL-2 carrying 563 bp full-length mIL-2-cDNA was constructed and was transferred into B16 melanoma cells by calcium phosphate copptn. method. After G418 resistance selection, limiting diln. and IL-2 assay, a clone secreting highest level of IL-2(506 U/mL) was selected, and then identified by Southern blot. The results demonstrated that IL-2 gene-transfected tumor cells exhibited unchanged in vitro growth but decreased tumorigenicity. A new type of tumor vaccine could be prepd. from the IL-2-secreting tumor cell clone established in the expt.

L27 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:707693 CAPLUS
DOCUMENT NUMBER: 123:167274
TITLE: Experimental study of the augmentation of host immune functions by fibroblast-mediated human interleukin-6 gene therapy
AUTHOR(S): Cao, Xuetao; Zhang, Weiping; Gu, Shen; Tao, Qun; Zhou, Zhengfang; Zheng, Lingli; Ye, Tianxing
CORPORATE SOURCE: Dep. Immunology, Second Military Medical Univ., Shanghai, 200433, Peop. Rep. China
SOURCE: Zhongguo Mianyixue Zazhi (1994), 10(1), 8-12
CODEN: ZMZAEE; ISSN: 1000-484X
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The effect of fibroblast-mediated hIL-6 gene therapy on the host immune functions was investigated. The results show that lymphocyte proliferation, IL-2 and IFN-gamma prodn., NK and LAK activity were enhanced significantly after in vivo implantation of IL-6 highly secreting fibroblast cell clone. It was suggested that fibroblast-mediated hIL-6 gene therapy could augment host immune function and outline a novel strategy for the biotherapy of cancer, reconstitution of hematopoiesis, etc.

L27 ANSWER 35 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1998:108073 BIOSIS
DOCUMENT NUMBER: PREV199800108073
TITLE: The enhancement or suppression of antitumor immune response by GM-CSF/IL-4 gene-modified tumor vaccine when immunized through different pathways.
AUTHOR(S): Zhu, Xuejun; Yu, Yizhi; Zhao, Yong; Tao, Qun; Ju, Dianwen; Zhang, Weiping; Cao, Xuetao
CORPORATE SOURCE: Dep. Immunol., Second Military Medical Univ., Shanghai 200433 China
SOURCE: Cancer Gene Therapy, (Nov.-Dec., 1997) Vol. 4, No. 6 CONF. SUPPL., pp. S57-S58.
Meeting Info.: Sixth International Conference on Gene Therapy of Cancer San Diego, California, USA November 20-22, 1997
ISSN: 0929-1903.
DOCUMENT TYPE: Conference
LANGUAGE: English

L27 ANSWER 36 OF 36 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1995:385737 BIOSIS
DOCUMENT NUMBER: PREV199598400037
TITLE: Therapeutic effect of IL-3 gene-transfected cellular
vaccine in combination with low dosage of cyclophosphamide
or IL-2 gene transfected vaccine.
AUTHOR(S): Cao, Xuetao; Zhang, Weiping; Xu,
Zhigong; Tao, Qun; Ye, Tianxing
CORPORATE SOURCE: Dep. Immunol., Second Military Med. Univ., Shanghai 200433
China
SOURCE: 9TH INTERNATIONAL CONGRESS OF IMMUNOLOGY.. (1995) pp. 867.
The 9th International Congress of Immunology.
Publisher: 9th International Congress of Immunology San
Francisco, California, USA.
Meeting Info.: Meeting Sponsored by the American
Association of Immunologists and the International Union of
Immunological Societies San Francisco, California, USA July
23-29, 1995
DOCUMENT TYPE: Conference
LANGUAGE: English

=> d que 114; d que 115; d que 120
L7 23481 SEA CD44 OR CD 44
L8 232730 SEA FELL
L9 80395 SEA HYALURON?
L12 2336 SEA L8(2A) (PROTEIN# OR GLYCOPROTEIN# OR PEPTIDE# OR POLYPEPTIDE
#)
L14 1 SEA (L7 OR L9) AND L12

L8 232730 SEA FELL
L15 5 SEA L8(W) (PROTEIN# OR GLYCOPROTEIN# OR PEPTIDE# OR POLYPEPTIDE#
)

L8 232730 SEA FELL
L9 80395 SEA HYALURON?
L18 5518 SEA L9(5A) BINDING
L20 3 SEA L18 AND L8

=> s 114 or 115 or 120
L28 9 L14 OR L15 OR L20

=> dup rem
ENTER # LIST OR (END):19
80395 ANSWERS REQUESTED EXCEEDS MAXIMUM ALLOWED OF 50000

=> dup rem 128
PROCESSING COMPLETED FOR L28
L29 8 DUP REM L28 (1 DUPLICATE REMOVED)
ANSWERS '1-5' FROM FILE DRUGU
ANSWERS '6-7' FROM FILE CAPLUS
ANSWER '8' FROM FILE BIOSIS

=> d kwic 129 1-8 *these are false drops*

L29 ANSWER 1 OF 8 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
AB To determine the roles of CD44 and hyaluronan in joint pathology, mice
with proteoglycan-induced arthritis were injected with equal amounts of 3
different anti-CD44 monoclonal antibodies (mAbs), which recognize

distinct epitopes of the receptor or the cell surface. Antibody IRAWB14.4 enhanced the ability of CD44 to interact with **hyaluronan** while mAb KM201 blocked ligand **binding**.

Antibody IM7.8.1 induced the shedding of CD44 from both murine and human cells. Treatment with both mAb IM7.8.1 and, to a lesser extent, mAb KM201, resulted in a decrease of joint swelling and a reduction of the number of inflammatory leukocytes in the synovia and joint cavities of arthritic animals.. . .

ABEX To determine the roles of CD44 and hyaluronan in joint pathology, mice with proteoglycan-induced arthritis were injected with equal amounts of 3 different anti-CD44 monoclonal antibodies (mAbs), which recognize distinct epitopes of the receptor or the cell surface. Antibody IRAWB14.4 enhances the ability of CD44 to interact with **hyaluronan** while mAb KM201 blocks ligand **binding**. Antibody IM7.8.1 does not block **hyaluronan binding** directly, but induces the shedding of CD44 from both murine and human cells. Treatment with both mAb IM7.8.1 and, to a lesser extent, mAb KM201, resulted in a decrease of joint swelling and a reduction of the number of inflammatory leukocytes in the synovia and joint cavities of arthritic animals. In contrast, ligand recognition-enhancing mAb IRAWB14.4 slightly increased the severity of arthritis in treated mice. Serum hyaluronan levels increased initially, then **fell** and remained low in IM7.8.1-treated animals. Injection of mAbs KM201 or IRAWB14.4 resulted in a slight decrease in serum hyaluronan concentrations without initial increase, and hyaluronan rapidly returned to original levels in these mice. (KJ)

L29 ANSWER 2 OF 8 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD

AB In male rats, chronic depot medroxyprogesterone acetate (DMPA) and testosterone enanthate (TE, Schering) (both i.m.) produced slight falls in testicular levels of **hyaluronidase** LDH sorbitol dehydrogenase (SDH), and acid (ACP), and alkaline phosphatase (ALP) and a more marked decrease in beta-glucuronidase. Testis cholesterol, lipid and protein content were also assayed. The biochemical changes correlated with ultrastructural testicular changes. These included degenerative changes in Golgi phase and late spermatids, and the presence of hypertrophied. . . .

ABEX. . . included mitochondrial hypertrophy of the midpieces, membrane lysis, absence of cristae, and degeneration of annulus leading to detachment of tail. 60 Day control rats showed slightly lower enzyme values than 30 day controls, and higher SDH (0.915 vs. 0.384 U/mg protein). 30 Day treated rats showed slight falls in beta-glucuronidase, **hyaluronidase**, LDH, ACP or ALP, and a slight rise in SDH vs. controls. 60 Day treated rats showed a slight rise in SDH, LDH, ACP and ALP, a slight fall in **hyaluronidase**, and a marked decrease in beta glucuronidase (3.25 vs. 74.72 ug/mg protein), vs. 60 day controls. Testicular cholesterol synthesis was unchanged despite a rise in total lipids after 30 days' treatment, but both were elevated after 60 days. Total testicular **proteins fell** slightly in both groups. Fertility was regained within a mean 45 and 68 days of 30 and 60 days' treatment, respectively, with restoration of testis weights to normalcy. Both groups fathered healthy pups, with a good survival rate. (W103/SJ)

CT COMB. *FT; I.M. *FT; RAT *FT; IN-VIVO *FT; TESTIS *FT; EC-3.2.1.36 *FT; EC-1.1.1.27 *FT; EC-1.1.1.14 *FT; EC-3.1.3.2 *FT; EC-3.1.3.1 *FT; EC-3.2.1.31 *FT; HISTOLOGY *FT; CONTRACEPTIVE *FT; CHOLESTEROL *FT; LIPID-METAB. *FT; PROTEIN-METAB. *FT; INJECTION *FT; LAB.ANIMAL *FT; **HYALURONOGLUCURONIDASE** *FT; LACTATE-DEHYDROGENASE *FT; L-IDITOL-DEHYDROGENASE *FT; ACID-PHOSPHATASE *FT; ALKALINE-PHOSPHATASE *FT; BETA-D-GLUCURONIDASE *FT

CT COMB. *FT; I.M. *FT; RAT *FT; IN-VIVO *FT; TESTIS *FT; EC-3.2.1.36 *FT; EC-1.1.1.27 *FT; EC-1.1.1.14 *FT; EC-3.1.3.2 *FT; EC-3.1.3.1 *FT; EC-3.2.1.31 *FT; HISTOLOGY *FT; CONTRACEPTIVE *FT; CHOLESTEROL *FT;

LIPID-METAB. *FT; PROTEIN-METAB. *FT; INJECTION *FT; LAB.ANIMAL *FT;
HYALURONOGLUCURONIDASE *FT; LACTATE-DEHYDROGENASE *FT;
L-IDITOL-DEHYDROGENASE *FT; ACID-PHOSPHATASE *FT; ALKALINE-PHOSPHATASE
*FT; BETA-D-GLUCURONIDASE *FT

L29 ANSWER 3 OF 8 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ABEX. . . salt-poor diet (50 mmol Na/day). Results There was a
significant fall in PGF2-alpha and PGE2 excretion via the urine.
Effective renal plasma flow was constant while GFR fell from 93.8 to 78.9
ml/min. The filtration fraction fell from 0.23 to 0.20 and this was
significant. Renin and aldosterone in plasma **fell**.
Protein excretion in the urine fell from 0.46 to zero. No
correlation existed between the fall in the GFR and the filtration
fraction on the 1 hand, and the fall in PGs on the other. (W43/PH)
(Effect van Indometacine op de Nierfunctie van Patienten met LED.)

L29 ANSWER 4 OF 8 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
AB Puromycin (PM, Calbiochem-Behring) inhibited (3H)serine and (35S)sulfate
incorporation into proteoglycans by cultures rat chondrosarcoma
chondrocytes. Molecular size of proteoglycans was increased by PM or
cycloheximide (Boehringer), but **hyaluronic** acid (HA)
binding or core protein size was unaltered. Only completed core
proteins are processed into proteoglycans by chondroitin sulfate (CS)
addition.
ABEX. . . (3H)serine or (35S) sulfate incorporation into 4M guanidine
extracts was determined. Proteoglycans were analyzed by density gradient
centrifugation, electrophoresis and Sepharose 6B chromatography. Some
extracts were incubated with chondroitinase ABC before separation. PM
(0.01-3 mM) inhibited (3H)serine and (35S)sulfate incorporation with IC50
of about 50 and 100 uM, respectively. Incorporation **fell**
rapidly for the first 2 hr of exposure and then more slowly. PM (0.1-1
mM) or 100 uM cycloheximide did not affect CS formation or processing of
already formed core proteins. Proteoglycans still aggregated with HA
when synthesis was inhibited by over 60% by 7-50 uM PM. Size of
proteoglycan. . .

L29 ANSWER 5 OF 8 DRUGU COPYRIGHT 2002 DERWENT INFORMATION LTD
ABEX. . . content and concentration both rose in regenerating liver. UDP-GT
rose 3-fold by day 0, returning to normal by day 7, as did DNA content,
but protein content/concentration remained raised. GOT, GPT and GLDH
were unchanged by pre-operative PB. Post-operative PB increased liver
regeneration by about 25% also, but DNA concentration **fell**;
protein content rose significantly, but concentration was
unchanged, as were GOT and GLDH. RNA/DNA ratio, GPT and UDP-GT were all
increased in regenerating liver.

L29 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AB Equil. dialysis in dil. soln. indicated that, in **hyaluronate**
oligosaccharide fraction (.apprx.18 residues) **binding** to pig
laryngeal cartilage proteoglycans, 1 mol. of the latter bound to each
proteoglycan monomer with dissocn. consts. (Kd) of 3 .times. 10-8 and 3
.times. 10-7M at 6 and 54.degree. resp., (pH 7.4, ionic strength
0.15-0.5). Aggregation was high at 6.degree., **fell** at
54.degree., but was largely recovered on cooling, indicating reversible
denaturation. The proportion of aggregation detd. by this method was
compared with results from gel chromatog. and ultracentrifugal techniques
with respect to underestn. of aggregatability. An oligosaccharide of
.apprx.56 residues bound >1 proteoglycan mol., and in **binding** of
670,000-mol.-wt. **hyaluronate**, ultracentrifugation indicated a Kd
of 2 .times. 10-7M in 0.5M guanidine-HCl at 20.degree..
ST **hyaluronate** oligosaccharide proteoglycan **binding**
IT Cartilage
(proteoglycans of, **hyaluronate** oligosaccharides

binding to)

IT Mucopolysaccharides, biological studies
RL: BIOL (Biological study)
(proteoglycans, **hyaluronate** oligosaccharides **binding**
to, of cartilage)

L29 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

AB . . . occurred. In (2), dry wt. decreased 50%, total N rose 23%,
alc.-sol. N at first rose and then fell 50% below the control, sol.
protein N rose 27%, and 95% of the buds swelled. In (3), 1-25 mg./l.
allowed some increase in water uptake, total N rose 44%, sol. N
fell, protein N rose, and bud growth was not reduced.
With 100-200 mg./l., however, water uptake dropped 40% and total N 21%,
sol. N rose 20% (synthesis inhibition), and protein N fell; buds were
inhibited 69 and 80%. In (4), water uptake dropped 22-47%, total N fell
12-24%, sol. N rose 18-81%, . . .

L29 ANSWER 8 OF 8 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1

AB. . . constant, which explains the decrease in Cl- concentration when the
HCO3- concentration increased. High doses of CCK (6670 and 13,335 ng kg-1
per h) and of caerulein (600 ng kg-1 per h strongly inhibited volume flow
and outputs of all the ions, and the sum of the concentrations of anions
fell. Protein concentration and output increased with
the same time course in response to both CCK and caerulein, i.e., a
sustained stimulation during infusion, without any delayed inhibitory
effect afterwards. The increase followed a linear dose-response relation
to both CCK and caerulein. Mean effective dose was .apprx. 1000 ng kg-1
per h. . .

=> d que 125

L7 23481 SEA CD44 OR CD 44
L9 80395 SEA HYALURON?
L18 5518 SEA L9(5A) BINDING
L24 42 SEA L7(W) LIKE
L25 14 SEA L24 AND L18

*since there were no ^{good} hits on
"FELL protein", searched for
CD44-like and hyaluron? binding
(in case same protein has
been studied but
given a different name)*

=> dup rem 125

PROCESSING COMPLETED FOR L25

L30 4 DUP REM L25 (10 DUPLICATES REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWER '3' FROM FILE CAPLUS
ANSWER '4' FROM FILE BIOSIS

=> d ibib ab 130 1-4

L30 ANSWER 1 OF 4 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2000123507 MEDLINE
DOCUMENT NUMBER: 20123507 PubMed ID: 10660111
TITLE: A role for the cell adhesion molecule CD44 and sulfation in
leukocyte-endothelial cell adhesion during an inflammatory
response?.
AUTHOR: Johnson P; Maiti A; Brown K L; Li R
CORPORATE SOURCE: Department of Microbiology & Immunology, University of
British Columbia, Vancouver, Canada..
pauline@interchange.ubc.ca
SOURCE: BIOCHEMICAL PHARMACOLOGY, (2000 Mar 1) 59 (5) 455-65. Ref:
113
Journal code: 9Z4; 0101032. ISSN: 0006-2952.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000302

AB CD44 is a widely expressed cell adhesion molecule that has been implicated in a variety of biological processes including lymphopoiesis, angiogenesis, wound healing, leukocyte extravasation at inflammatory sites, and tumor metastasis. The adhesive function of **CD44**, like other molecules involved in inducible adhesion, is tightly regulated. Post-translational modifications, isoform expression, aggregation state, and protein associations all can affect the ligand binding properties of CD44, and these can vary depending on the cell type and the activation state of the cell. The most extensively characterized ligand for CD44 is hyaluronan, a component of the extracellular matrix. Interactions between CD44 and hyaluronan can mediate both cell-cell and cell-extracellular matrix adhesion. In the immune system, both the selectin molecules and CD44 have been implicated in the initial binding of leukocytes to endothelial cells at an inflammatory site. Sulfation is required for selectin-mediated leukocyte-endothelial cell interactions, and, recently, inducible sulfation also was shown to regulate CD44-mediated leukocyte adhesion to endothelial cells. Sulfation, therefore, may be important in the regulation of cell adhesion at inflammatory sites. In this commentary we have reviewed the molecular aspects of CD44 and the mechanisms that regulate its **binding to hyaluronan**. In addition, we have summarized the role of CD44 and hyaluronan in mediating leukocyte-endothelial cell interactions and have discussed how this interaction may be regulated. Finally, we examined the potential role of sulfation as an inducible means to regulate CD44-mediated leukocyte adhesion and as a more general mechanism to regulate leukocyte-endothelial cell interactions.

L30 ANSWER 2 OF 4 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 93024389 MEDLINE
DOCUMENT NUMBER: 93024389 PubMed ID: 1406635
TITLE: A **CD44-like** endothelial cell transmembrane glycoprotein (GP116) interacts with extracellular matrix and ankyrin.
AUTHOR: Bourguignon L Y; Lokeshwar V B; He J; Chen X; Bourguignon G J
CORPORATE SOURCE: Department of Cell Biology, School of Medicine, University of Miami, Florida 33101.
CONTRACT NUMBER: GM 36353 (NIGMS)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1992 Oct) 12 (10) 4464-71. Journal code: NGY; 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
LANGUAGE: Journal; Article; (JOURNAL ARTICLE)
FILE SEGMENT: English
ENTRY MONTH: Priority Journals
ENTRY DATE: 199210
Entered STN: 19930122
Last Updated on STN: 19930122
Entered Medline: 19921026

AB We used complementary biochemical and immunological techniques to establish that an endothelial cell transmembrane glycoprotein, GP116, is a **CD44-like** molecule and binds directly both to extracellular matrix components (e.g., hyaluronic acid) and to ankyrin. The specific characteristics of GP116 are as follows: (i) GP116 can be surface labeled with Na 125I and contains a wheat germ agglutinin-binding site(s), indicating that it has an extracellular domain; (ii) GP116 displays immunological cross-reactivity with a panel of CD44 antibodies,

shares some peptide similarity with CD44, and has a similar 52-kDa precursor molecule, indicating that it is a **CD44-like** molecule; (iii) GP116 displays specific **hyaluronic acid-binding** properties, indicating that it is a hyaluronic acid receptor; (iv) GP116 can be phosphorylated by endogenous protein kinase C activated by 12-O-tetradecanoylphorbol-13-acetate and by exogenously added protein kinase C; and (v) GP116 and a 20-kDa tryptic polypeptide fragment of GP116 from the intracellular domain are capable of binding the membrane-cytoskeleton linker molecule, ankyrin. Furthermore, phosphorylation of GP116 by protein kinase C significantly enhances GP116 binding to ankyrin. Together, these findings strongly suggest that phosphorylation of the transmembrane glycoprotein GP116 (a **CD44-like** molecule) by protein kinase C is required for effective GP116-ankyrin interaction during endothelial cell adhesion events.

L30 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:537916 CAPLUS
DOCUMENT NUMBER: 131:154496
TITLE: Protein and DNA sequences encoding a human **CD44-like** protein
INVENTOR(S): Ni, Jian; Gentz, Reiner L.; Dillon, Patrick J.
PATENT ASSIGNEE(S): Human Genome Sciences, Inc., USA
SOURCE: U.S., 38 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| US 5942417 | A | 19990824 | US 1997-892880 | 19970715 |

PRIORITY APPLN. INFO.: US 1996-21762P P 19960715

AB The invention provides protein and DNA sequences of a novel **CD44-like** protein, which is about 24% identical and about 46% similar to rat CD44. CD44 is known to act as a receptor for hyaluronan, and the protein of the present invention is able to bind hyaluronan as well. The invention further relates to screening methods for identifying agonists and antagonists capable of enhancing or inhibiting **CD44-like** protein-mediated signaling, and therapeutic methods for treating diseases assocd. with said signaling.

REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1993:17916 BIOSIS
DOCUMENT NUMBER: PREV199344006116
TITLE: Endothelial cell transmembrane glycoprotein, GP116 (A **CD44-like** molecule) contains **hyaluronic acid (HA) binding** site and links to ankyrin.
AUTHOR(S): Lokeshwar, Vinata B.; Dominguez, Rafael; Bourguignon, Gerard J.; Bourguignon, Lilly Y. W.
CORPORATE SOURCE: Dep. Cell Biology Anatomy, University Miami Medical School, Miami, Fla. 33101
SOURCE: Molecular Biology of the Cell, (1992) Vol. 3, No. SUPPL., pp. 73A.
Meeting Info.: Thirty-second Annual Meeting of the American Society for Cell Biology, Denver, Colorado, USA, November 15-19, 1992. MOL BIOL CELL
ISSN: 1059-1524.
DOCUMENT TYPE: Conference
LANGUAGE: English

=> fil biotechds scisearch wpids

FILE 'BIOTECHDS' ENTERED AT 10:37:23 ON 25 MAR 2002

COPYRIGHT (C) 2002 DERWENT INFORMATION LTD AND INSTITUTE FOR SCIENTIFIC INFORMATION

FILE 'SCISEARCH' ENTERED AT 10:37:23 ON 25 MAR 2002

COPYRIGHT (C) 2002 Institute for Scientific Information (ISI) (R)

FILE 'WPIDS' ENTERED AT 10:37:23 ON 25 MAR 2002

COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

=> d que 140

L31 174 SEA TAO Q?/AU
L32 6286 SEA ZHANG W?/AU
L33 1251 SEA CAO X?/AU
L34 4105 SEA CD44 OR CD 44
L35 21931 SEA FELL
L37 880 SEA HYALURON?(5A) BINDING
L38 19 SEA L31 AND L32 AND L33
L40 0 SEA L38 AND (L34 OR L35 OR L37)

=> d que 136; d que 142; s 136 or 142

L35 21931 SEA FELL
L36 1 SEA L35(W) ?PROTEIN?

L34 4105 SEA CD44 OR CD 44
L37 880 SEA HYALURON?(5A) BINDING
L41 9 SEA L34(W) LIKE
L42 3 SEA L37 AND L41

L45 4 L36 OR L42

=> dup rem 145

PROCESSING COMPLETED FOR L45

L46 4 DUP REM L45 (0 DUPLICATES REMOVED)
ANSWERS '1-4' FROM FILE SCISEARCH

=> d ibib ab 1-4; d que 144

L46 ANSWER 1 OF 4 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 2000:78871 SCISEARCH

THE GENUINE ARTICLE: 276VT

TITLE: A role for the cell adhesion molecule CD44 and sulfation
in leukocyte-endothelial cell adhesion during an
inflammatory response?

AUTHOR: Johnson P (Reprint); Maiti A; Brown K L; Li R

CORPORATE SOURCE: UNIV BRITISH COLUMBIA, DEPT MICROBIOL & IMMUNOL, 300-6174
UNIV BLVD, VANCOUVER, BC V6T 1Z3, CANADA (Reprint)

COUNTRY OF AUTHOR: CANADA

SOURCE: BIOCHEMICAL PHARMACOLOGY, (1 MAR 2000) Vol. 59, No. 5, pp.
455-465.

Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD,
LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.

ISSN: 0006-2952.

DOCUMENT TYPE: General Review; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 112

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB CD44 is a widely expressed cell adhesion molecule that has been implicated in a variety of biological processes including lymphopoiesis, angiogenesis, wound healing, leukocyte extravasation at inflammatory sites, and tumor metastasis. The adhesive function of **CD44**, like other molecules involved in inducible adhesion, is tightly regulated. Post-translational modifications, isoform expression, aggregation state, and protein associations all can affect the ligand binding properties of CD44, and these can vary depending on the cell type and the activation state of the cell. The most extensively characterized ligand for CD44 is hyaluronan, a component of the extracellular matrix. Interactions between CD44 and hyaluronan can mediate both cell-cell and cell-extracellular matrix adhesion. In the immune system, both the selectin molecules and CD44 have been implicated in the initial binding of leukocytes to endothelial cells at an inflammatory site. Sulfation is required for selectin-mediated leukocyte-endothelial cell interactions, and, recently, inducible sulfation also was shown to regulate CD44-mediated leukocyte adhesion re, endothelial cells. Sulfation, therefore, may be important in the regulation of cell adhesion at inflammatory sites. In this commentary we have reviewed the molecular aspects of CD44 and the mechanisms that regulate its **binding to hyaluronan**. In addition, we have summarized the role of CD44 and hyaluronan in mediating leukocyte-endothelial cell interactions and have discussed how this interaction may be regulated. Finally, we examined the potential role of sulfation as an inducible means to regulate CD44-mediated leukocyte adhesion and as a more general mechanism to regulate leukocyte-endothelial cell interactions. (C) 2000 Elsevier Science Inc.

L46 ANSWER 2 OF 4 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 95:22685 SCISEARCH

THE GENUINE ARTICLE: PY294

TITLE: THE DNA-ACTIVATED PROTEIN-KINASE IS REQUIRED FOR THE PHOSPHORYLATION OF REPLICATION PROTEIN-A DURING SIMIAN-VIRUS-40 DNA-REPLICATION

AUTHOR: BRUSH G S; ANDERSON C W; KELLY T J (Reprint)

CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, DEPT MOLEC BIOL & GENET, BALTIMORE, MD, 21205 (Reprint); JOHNS HOPKINS UNIV, SCH MED, DEPT MOLEC BIOL & GENET, BALTIMORE, MD, 21205; BROOKHAVEN NATL LAB, DEPT BIOL, UPTON, NY, 11973

COUNTRY OF AUTHOR: USA

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (20 DEC 1994) Vol. 91, No. 26, pp. 12520-12524.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 32

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The 32-kDa subunit of replication protein A (RPA) is phosphorylated during the S phase of the cell cycle in vivo and during simian virus 40 DNA replication in vitro. To explore the functional significance of this modification, we purified a HeLa **cell protein kinase** that phosphorylates RPA in the presence of single-stranded DNA. By several criteria we identified the purified enzyme as a form of the DNA-activated protein kinase (DNA-PK), a previously described high molecular weight protein kinase that is capable of phosphorylating a number of nuclear DNA binding proteins. Phosphorylation of RPA by DNA-PK is stimulated by natural single-stranded DNAs but not by homopolymers lacking secondary structure. Studies with the simian virus 40 model system indicate that DNA-PK is required for DNA-replication-dependent RPA phosphorylation. Depletion of the kinase activity, however, has no effect on the extent of

DNA replication in vitro. Our data support a model in which phosphorylation of RPA by DNA-Pk is activated by formation of replication intermediates containing single- and double-stranded regions. This event may be involved in a signaling mechanism that coordinates DNA replication with the cell cycle.

L46 ANSWER 3 OF 4 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 92:573508 SCISEARCH

THE GENUINE ARTICLE: JP798

TITLE: A **CD44-LIKE** ENDOTHELIAL-CELL
TRANSMEMBRANE GLYCOPROTEIN (GP116) INTERACTS WITH
EXTRACELLULAR-MATRIX AND ANKYRIN

AUTHOR: BOURGUIGNON L Y W (Reprint); LOKESHWAR V B; HE J; CHEN X;
BOURGUIGNON G J

CORPORATE SOURCE: UNIV MIAMI, SCH MED, DEPT CELL BIOL & ANAT, MIAMI, FL,
33101 (Reprint); UNIV MIAMI, SCH MED, DEPT DERMATOL,
MIAMI, FL, 33101

COUNTRY OF AUTHOR: USA

SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (OCT 1992) Vol. 12, No.
10, pp. 4464-4471.
ISSN: 0270-7306.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 40

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB We used complementary biochemical and immunological techniques to establish that an endothelial cell transmembrane glycoprotein, GP116, is a **CD44-like** molecule and binds directly both to extracellular matrix components (e.g., hyaluronic acid) and to ankyrin. The specific characteristics of GP116 are as follows: (i) GP116 can be surface labeled with Na I-125 and contains a wheat germ agglutinin-binding site(s), indicating that it has an extracellular domain; (ii) GP116 displays immunological cross-reactivity with a panel of CD44 antibodies, shares some peptide similarity with CD44, and has a similar 52-kDa precursor molecule, indicating that it is a **CD44-like** molecule; (iii) GP116 displays specific **hyaluronic acid-binding** properties, indicating that it is a hyaluronic acid receptor; (iv) GP116 can be phosphorylated by endogenous protein kinase C activated by 12-O-tetradecanoylphorbol-13-acetate and by exogenously added protein kinase C; and (v) GP116 and a 20-kDa tryptic polypeptide fragment of GP116 from the intracellular domain are capable of binding the membrane-cytoskeleton linker molecule, ankyrin. Furthermore, phosphorylation of GP116 by protein kinase C significantly enhances GP116 binding to ankyrin. Together, these findings strongly suggest that phosphorylation of the transmembrane glycoprotein GP116 (a **CD44-like** molecule) by protein kinase C is required for effective GP116-ankyrin interaction during endothelial cell adhesion events.

L46 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2002 ISI (R)

ACCESSION NUMBER: 92:590666 SCISEARCH

THE GENUINE ARTICLE: JR255

TITLE: ENDOTHELIAL-CELL TRANSMEMBRANE GLYCOPROTEIN, GP116 (A
CD44-LIKE MOLECULE) CONTAINS
HYALURONIC-ACID (HA) BINDING-SITE AND
LINKS TO ANKYRIN

AUTHOR: LOKESHWAR V B (Reprint); DOMINGUEZ R; BOURGUIGNON G J;
BOURGUIGNON L Y W

CORPORATE SOURCE: UNIV MIAMI, SCH MED, DEPT CELL BIOL & ANAT, MIAMI, FL,
33101

COUNTRY OF AUTHOR: USA

SOURCE: MOLECULAR BIOLOGY OF THE CELL, (SEP 1992) Vol. 3, Supp. S,
pp. A73.

DOCUMENT TYPE: ISSN: 1059-1524.
FILE SEGMENT: Conference; Journal
LANGUAGE: LIFE
REFERENCE COUNT: ENGLISH
No References

L34 4105 SEA CD44 OR CD 44
L35 21931 SEA FELL
L37 880 SEA HYALURON?(5A) BINDING
L44 8 SEA L35 AND (L34 OR L37)

=> dup rem 144

PROCESSING COMPLETED FOR L44

L47 8 DUP REM L44 (0 DUPLICATES REMOVED)
ANSWERS '1-8' FROM FILE SCISEARCH

=> d kwic 147 1-8 *these are false drops (it appears that "fell" is a typographical error for "cell" in several of these)*

L47 ANSWER 1 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)
AB . . . correlates of protective immunity will facilitate the design and assessment of new candidate vaccines. Therefore, we investigated the kinetics of the CD4(+) T cell response and IFN-gamma production in an intravenous challenge model of Mycobacterium bovis bacille Calmette-Guerin (BCG) before and after DNA immunization. Activated/memory CD4(+) T cells, defined as **CD44**(hi)CD45RB(lo) expanded following infection, peaking at 3-4 weeks, and decreased as the bacterial load **fell**. Activated/memory CD4(+) T cells were the major source of IFN-gamma and the level of antigen-specific IFN-gamma-secreting lymphocytes, detected by ELISPOT, paralleled the changes in bacterial load. To examine the effects of a DNA vaccine, we immunized mice with a plasmid expressing the mycobacterial secreted antigen 85B (Ag85B). This led to. . .

L47 ANSWER 2 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)
AB Epithelioid sarcoma (ES) is a very aggressive soft-tissue tumor in vivo, but no experimental data on its invasive and metastatic behavior have been reported. In the present study, 3 different clonal sub-populations (GRU-IA, GRU-IB and GRU-IC), derived from the same human ES **fell** line, GRU-I, were investigated for in vitro invasiveness in relation to migration, adhesion and the expression of different invasion- and metastasis-related genes. Tumor spheroids of GRU-IA were markedly more invasive in the chick-heart invasion assay (CHIA) than spheroids of GRU-IB and GRU-IC. These results were paralleled by a significantly higher. . . result mainly from differences in motility, but also partly depend on differences in cell-cell adhesion. On the molecular level, low invasive potential was associated with over-expression of distinct tissue inhibitor of metalloproteinases (TIMPs) relative to matrix metalloproteinase-2 and -9. However, no association was found between invasion and the expression of **CD44** splicing variants or nm23 isoforms. Our results suggest that differences in invasion between GRU-IA, GRU-IB and GRU-IC are caused mainly by interclonal differences in migration, and might result from differences in the expression of distinct (C) 1999 Wiley-Liss, Inc.

L47 ANSWER 3 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)
AB Lectins or agglutinins are proteins with affinity for specific sugar residues. Peanut agglutinin (PNA) and the lectin from the edible mushroom (Agaricus bisporus, ABL) both bind to the disaccharide galactosyl beta-1,3-N-acetyl galactosamine alpha-. This is expressed in keratinocytes as an O-linked chain on **CD44**, a polymorphic membrane glycoprotein. Many lectins are mitogens and PNA is a mitogen for colonic

epithelial cells. However, ABL reversibly inhibits proliferation of colonic cancer cell lines without cytotoxicity and thus has therapeutic potential in situations such as psoriasis where proliferation is increased. We have therefore investigated the effect of . . . erythema, blood flow or thickness compared with vehicle or baseline (n = 6). ABL 0.1% in white soft paraffin was compared with vehicle in 11 psoriatic patients, using comparative contralateral plaques. Twice daily application for 2 weeks showed no significant difference from vehicle-treated sites, although the skin thickness of plaques fell from 5.3 +/- 0.4 (n = 11, mean +/- SEM) to 4.1 +/- 0.3 mm. in view of the in vitro results further studies are warranted, particularly if means can be found to improve the epidermal penetration of the relatively large ABL molecule (60 kDa).

STP KeyWords Plus (R): HUMAN EPIDERMAL-KERATINOCYTES; PEANUT LECTIN; BINDING GLYCOPROTEINS; INVITRO; GROWTH; DIFFERENTIATION; EXPRESSION; INVIVO; CD44

L47 ANSWER 4 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)

AB . . . bone cells and which is expressed more abundantly in osteocytes than in osteoblasts, From these transgenic mice, we isolated cells from tile long bones using sequential collagenase digestion and maintained these cells on collagen-coated surfaces which are optimal for osteocyte maintenance and growth. We describe here the properties of a fell line cloned from these cultures, called MLO-Y4 (for murine long bone osteocyte Y4), The properties of MLO-Y4 cells are very similar to primary osteocytes. Like primary osteocytes and unlike primary osteoblasts, the cell line produces large amounts of osteocalcin but low amounts of alkaline phosphatase, The cells produce extensive, complex; dendritic processes and are positive for T-antigen, for osteopontin, for the neural antigen CD44, and for connexin 43, a protein found in gap junctions, This cell line also produces very small amounts of type I collagen mRNA compared with primary osteoblasts, MLO-Y4 cells lack detectable mRNA for osteoblast-specific factor 2, which appears to be a positive marker for osteoblasts but may be a negative. . .

L47 ANSWER 5 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)

TI Antibodies to CD44 enhance adhesion of normal CD34(+) cells and acute myeloblastic but not lymphoblastic leukaemia cells to bone marrow stroma

AB The role of CD44 in the adhesion of haemopoietic cells to bone marrow stromal layers has not been clearly defined in humans, although its importance in the murine system has been well documented We have demonstrated that the CD44 antibody, NIH44-1, enhances the adhesion of haemopoietic cells to bone marrow stroma, Normal human CD34(+) haemopoietic progenitors and blasts from patients with acute myeloblastic, but not lymphoblastic, leukaemia responded to NIH44-1. All CD44 antibodies tested which bound the same epitope as NM44-1 also augmented haemopoietic fell adhesion to bone marrow adherent layers: however, antibodies which bound to other CD44 epitopes showed mixed responses. Augmented adhesion was independent of cell metabolism, suggesting that antibody binding resulted in direct activation of the CD44 molecule, However, hyaluronic acid was not the ligand for induced adhesion, nor could we show a role for other CD44 ligands including fibronectin, laminin, collagen or chondroitin sulphate proteoglycan. Similarly none of the 22 CD44 antibodies tested inhibited the stimulatory effect of the NIH44-1. Expression of CD44 was not sufficient to determine NM44-1 responsiveness since cell lines and leukaemic tells which failed to respond to NIH44-1 expressed high levels of CD44. Neither CD44 isoforms nor glycosylation patterns could be identified as predictive of response. CD44 antibodies enhanced binding of normal and leukaemic haemopoietic progenitors to bone marrow fibroblasts via an unidentified stromal ligand.

ST Author Keywords: **CD44**; leukaemia; adhesion; bone marrow stroma; haemopoiesis

L47 ANSWER 6 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)
TI Evaluation of soluble **CD44** splice variant v5 in the diagnosis

and follow-up in breast cancer patients

AB Aberrant expression of **CD44** splice variants has been detected on a variety of human tumor cells. Overexpression of specific isoforms has been shown to be associated with metastasis and poor prognosis in breast cancer. We evaluated the possible utility of soluble **CD44** splice variant v5 (sCD44v5) as a circulating, tumor-associated marker in breast cancer patients. Serum levels of sCD44v5 were determined in 147 healthy volunteers, in 53 patients with nonmalignant breast disease, in 85 patients with breast cancer at presentation, in 13 patients with recurrence and in 73 patients with active metastatic. . . . showed considerable between-patient variation while the intrapatient levels remained within relatively narrow limits. In patients with active metastatic disease, elevated levels of sCD44v5 (>58 ng.ml(-1)) were detected in 50% of the cases with marked elevation in only 26%. In these cases, sCD44v5 correlated with the extent of metastatic disease and fell during clinical response to cytoreductive therapy. In comparison with CA15-3 in the patients' follow-up serum levels of sCD44v5 proved to be much less sensitive concerning lead time, percentage of raised serum levels at the time of recurrence and in metastatic disease. The value of sCD44v5 determinations in breast cancer patients. . . .

L47 ANSWER 7 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)
AB Blood leucocyte subsets in neonatally (20-day-old) thymectomized (Tx)

and sham-thymectomized (STx) pigs were analysed 13 times over nearly 2 years. Tx piglets showed a persistent selective leucopenia, due mainly to a similar to 95% reduction in gamma delta null T cells which fell , with a circulating half-life of similar to 2 weeks, to similar to 0.3 x 10(6)/ml. This residual population was extrathymic in origin since it increased numerically at least similar to eightfold as the Tx pigs grew. Changes in other subsets were complex and affected by antigenic experience associated with weaning. . . . 3.5-fold in Tx pigs. This was largely due to an increase in CD2(+) CD8(+) MHC class II+ T cells, particularly in Tx pigs. The small residual thymus-independent gamma delta null subset also increased, while gamma delta T cells in STx pigs actually decreased. Evolving changes in expression of CD45, CD45R, **CD44**, CD18 and very late antigen type-4 (VLA-4) also occurred following thymectomy. Thus, the most persistent long-term effect of thymectomy, other than the lack of gamma delta null T cells, was the markedly increased numbers of double-positive (CD4(+)CD8(low)) T cells, most of which expressed MHC class II and higher levels of. . . .

L47 ANSWER 8 OF 8 SCISEARCH COPYRIGHT 2002 ISI (R)
AB The role of cell adhesion molecules (CAM) LFA1, ICAM-1, LFA3, VLA1,

VLA4, CD29, **CD44**, and CD56 in tumor-infiltrating lymphocyte (TIL) and natural killer cell (NK)-mediated killing of target cells was studied. Melanoma cell lines and autologous TIL were derived from seven patients with metastatic melanoma, and cytotoxicity assays were done in the presence and absence of monoclonal antibodies (MoAb) to CAM expressed on melanoma cells or TIL. The melanoma cell lines analyzed were all positive for CD29 and LFA3 expression, negative for LFA1 expression, but showed variable expression of ICAM-1, VLA1, VLA4, **CD44**, and CD56. The effects of anti-CAM antibodies on TIL-mediated melanoma killing fell into three categories: (1) consistent inhibition of TIL-mediated killing was observed when melanoma cells were pretreated with anti-ICAM1 and anti-LFA-3 MoAb or when TIL were pretreated with anti-LFA1; (2) no effect was observed when melanoma cells were pretreated with anti-CD56; or (3) a discreet, but significant, inhibition was observed when target cells were pretreated with anti-CD29, anti-VLA1, anti-VLA4,

and anti-CD44. Cytotoxicity was significantly enhanced by pretreatment of target cells with gamma-interferon (gamma-IFN), although gamma-IFN did not augment surface expression of the CAM studied. The NK-mediated killing of K562 cells was blocked by anti-LFA1, anti-CD18, and anti-ICAM, and partially inhibited by anti-CD44 MoAb. Together, these results suggest that several accessory CAM may play a role in regulating cellular cytotoxicity. Because cytotoxicity generally correlated with the level of expression of CAM in melanoma cells, weak CAM surface expression may provide a means for melanomas to escape immune surveillance.

THIS PAGE BLANK (USPTO)